

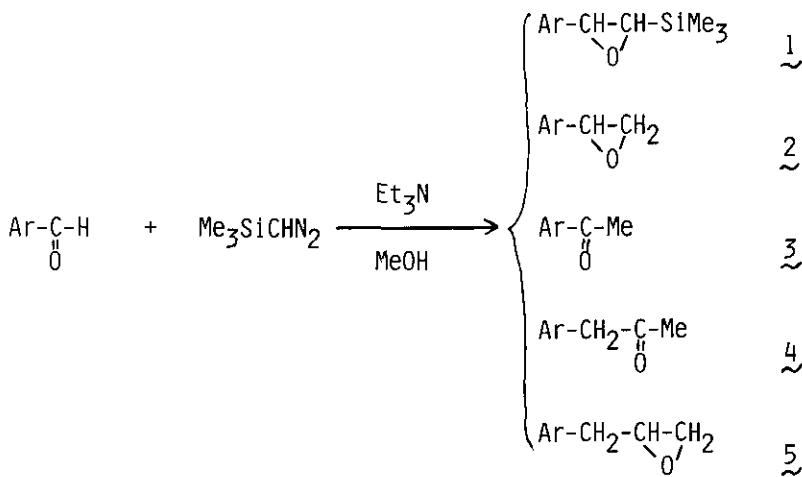
NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. II.¹
 REACTION OF TRIMETHYLSILYL DIAZOMETHANE WITH AROMATIC ALDEHYDES

Norio Hashimoto, Toyohiko Aoyama, and Takayuki Shioiri *

Faculty of Pharmaceutical Sciences, Nagoya City University,
 Tanabe-dori, Mizuho-ku, Nagoya 467, JAPAN

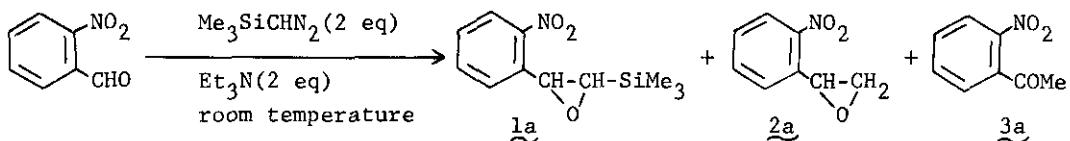
Abstract—Trimethylsilyldiazomethane adds to aromatic aldehydes in the presence of triethylamine in methanolic solution to give epoxides and homologous compounds.

We have already proposed the use of trimethylsilyldiazomethane (TMSCN_2) as a stable and safe substitute for highly toxic and explosive diazomethane in the homologation of ketones¹ as well as carboxylic acids.² Although various ketones smoothly react with TMSCN_2 in the presence of boron trifluoride etherate to give homologated ketones,¹ the reaction of aromatic aldehydes with TMSCN_2 ³ under similar reaction conditions has resulted in the formation of a complicated mixture of products. Further investigations along this line, however, have revealed that TMSCN_2 reacts with aromatic aldehydes in the presence of triethylamine in methanolic solution to give epoxides 1 and 2 and homologous compounds 3~5. The products depend on the solvent and on the substituents in the aromatic ring.



Treatment of 2-nitrobenzaldehyde with TMSClN_2 ⁴ in methanol-hexane(1:19) containing triethylamine at room temperature with protection of light gave the silylepoxyde 1a^{5,6} and the epoxide 2a after a separation on a silica gel column. The increase of the methanol content in the reaction solvent accelerated the reaction rate with decreasing the yield of 1a but increasing the yield of 2a. Since 1a could not be converted to 2a by the treatment with methanol or silica gel, 2a was not produced from 1a. On the other hand, TMSClN_2 reacted with tetradeuteriomethanol to generate a gas, and the yellow color of TMSClN_2 was decolorized. After 5 h, the methine proton of TMSClN_2 at 2.80 ppm in its nmr spectrum completely disappeared. Thus, the actual reaction species in the solvent containing methanol will be a mixture of TMSClN_2 and diazomethane derived by the action of TMSClN_2 with methanol.⁷ Reaction of 2-nitrobenzaldehyde with diazomethane will give the epoxide 2a.⁸ The ratio of TMSClN_2 and diazomethane generated depends on the solvent used and the content of methanol. The increase of the polarity of the co-solvent decreases the ratio of 1a to 2a, as shown in Table 1. A small amount of 2-nitroacetophenone(3a) was also formed in some cases.

Table 1.



Solvent	Time, h	Yield of Products, %		
		<u>1a</u>	<u>2a</u>	<u>3a</u>
MeOH-Hexane(1:19)	43	54	18	-
MeOH-Hexane(1:4)	27	39	34	5
MeOH-Hexane(1:1)	3	trace	72	8
MeOH-Benzene(1:4) ^a	25	44	13	- ^b
MeOH-CH ₂ Cl ₂ (1:4) ^{a,c}	29	46	26	-
MeOH-Et ₂ O(1:4)	26	14	52	8 ^d

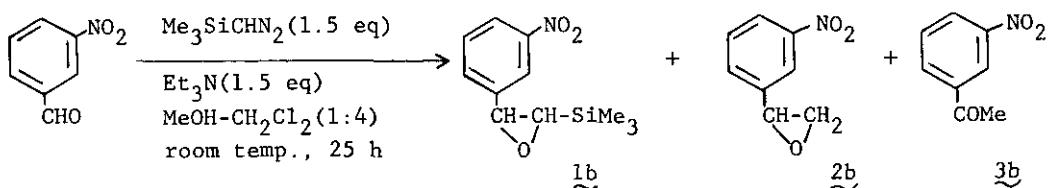
a: 1.5 Eq. of TMSClN_2 was used.

b: The starting aldehyde was recovered in 19 % yield.

c: 1.5 Eq. of triethylamine was used.

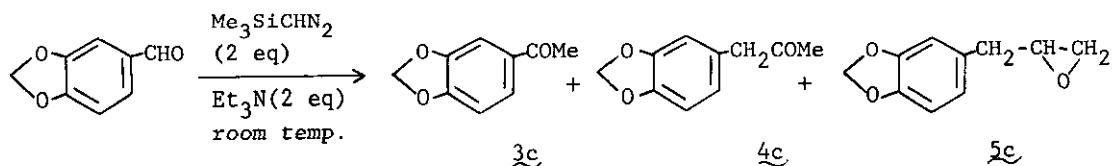
d: The starting aldehyde was recovered in 7 % yield.

3-Nitrobenzaldehyde has been reported⁸ to give 3-nitroacetophenone (3b) in 30 % yield by the reaction with diazomethane in methanol-diethyl ether. But the reaction with TMSClN_2 under similar reaction conditions to the above in methanol-methylene chloride(1:4) afforded the silylepoxyde 1b⁹ in 24.5 % yield, the epoxide 2b in 19 % yield, and 3-nitroacetophenone (3b) in 25 % yield.



The reaction of piperonal with TMSClN_2 in methanolic solution furnished the homologous ketones 3c and 4c and the epoxide 5c, but no epoxides as 1 and 2 were obtained, as shown in Table 2. Presumably, the electron-donating substituent in the aromatic nucleus will retard the reaction with TMSClN_2 which may have a lower nucleophilicity than diazomethane. Hence, TMSClN_2 will react first with methanol and then the generated diazomethane will add to piperonal, the result of which is quite similar to the reported result¹⁰ on the reaction of piperonal with diazomethane in methanol-diethyl ether. In the case of the reaction with TMSClN_2 , however, it should be noted that triethylamine as well as methanol is essential to conduct the reaction.

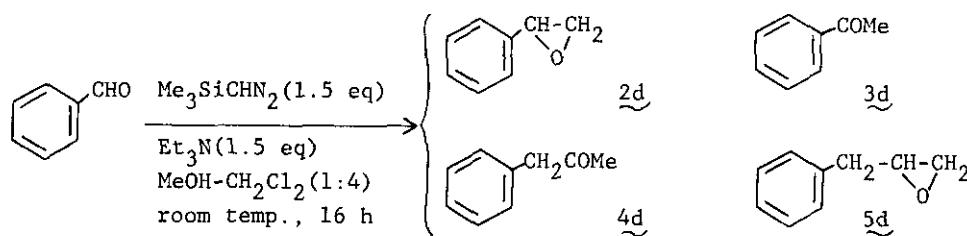
Table 2.



Solvent	Time, h	Yield of Products, %		
		<u>3c</u>	<u>4c</u>	<u>5c</u>
MeOH- CH_2Cl_2 (1:4)	24	17	34	14
MeOH- Et_2O (1:5)	24	19	37	9
MeOH- Et_2O ¹⁰	2-4 days ^a	7	21	7

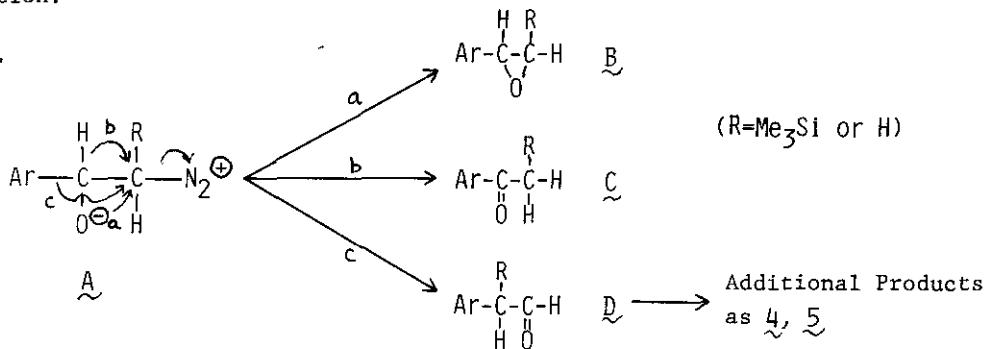
a: The reaction was carried out at -15° .

Finally, benzaldehyde afforded a mixture of 2d(12 %), 3d(15 %), 4d(37 %), and 5d(12 %) under similar reaction conditions.



Intermediates of the above reactions will be depicted as the general formula A³ in the Scheme 1. The betaine A will easily lose nitrogen, followed by the intramolecular attack with (a) the oxygen anion, (b) the hydride, or (c) the aryl group to give the epoxide B, the ketone C, or the aldehyde D, respectively. The aldehyde D will be further transformed with diazomethane to give the ketone 4 and/or the epoxide 5. The electron-donating function in the aromatic nucleus as the methylene-dioxy function of piperonal will facilitate the 1,2-shift of the aromatic ring as shown by the arrow c. On the contrary, the electron-withdrawing function as the nitro function will favor the attack of the oxygen anion as shown by the arrow a. Furthermore, even if the α -trimethylsilyl derivatives of the ketone C or the aldehyde D will be once formed, they will be easily transformed to the ketone C(R=H) or the aldehyde D(R=H) by the action of methanol or the aqueous work-up after the reaction.

Scheme 1.



Thus, the reaction of aromatic aldehydes with TMSCHN_2 under the co-existence of methanol and triethylamine will be of great mechanistic interest though it may be of little preparative value.

Acknowledgement

One of the authors (N.H.) is grateful to the Miyata Research Foundation for a research fellowship.

References and Notes

1. Part 10, N. Hashimoto, T. Aoyama, and T. Shioiri, Tetrahedron Lett., submitted.
2. T. Aoyama and T. Shioiri, Tetrahedron Lett., submitted.
3. The reaction of diazomethane with aldehydes has been discussed in detail, see
(a) J.S. Pizey, 'Synthetic Reagents', Vol. II, Ellis Horwood Ltd., Chichester, 1974, Chapter 2; (b) C.D. Gutsche, Org. Reactions, 1954, 8, 364.
4. TMSCHN_2 was prepared by the Seyferth's method, D. Seyferth, H. Menzel, A.W. Dow, and T.C. Flood, J. Organomet. Chem., 1972, 44, 279, which we slightly modified. The actual reagent used has been a mixture of TMSCHN_2 and hexamethyldisiloxane(7:3), the latter of which has no influence on the reaction. For a recent improved procedure for the preparation of TMSCHN_2 , see T.J. Barton and S.K. Hoekman, Synth. React. Inorg. Metal-Org. Chem., 1979, 9, 297.
5. New compounds have been identified by ir and nmr measurements as well as elemental analysis. Known compounds have been identified by spectral comparisons with the authentic samples.
6. The stereochemistry of 1a will be trans, which was judged from the J -value (3.50 Hz) of its nmr spectrum; Cf. J.J. Eisch and J.E. Galle, J. Org. Chem., 1976, 41, 2615.
7. The reaction of TMSCHN_2 with methanol in the dark has been reported to give trimethylmethoxysilane(~100 %) and dimethyl ether(~100 %) fairly rapidly; R.L. Kreeger and H. Shechter, Tetrahedron Lett., 1975, 2061.
8. In fact, the reaction of 2-nitrobenzaldehyde with diazomethane has been reported to give 2a and 3a in 65 and 16 % yields, respectively; F. Arndt, J. Amende, and W. Ender, Monatsh., 1932, 59, 202.
9. The stereochemistry of 1b will be trans, which was judged from the J -value (3.3 Hz) of its nmr spectrum.
10. E. Mosettig, Chem. Ber., 1929, 62, 1271.

Received, 3rd September, 1980